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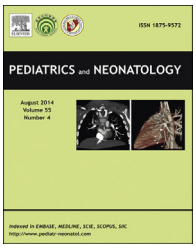

ORIGINAL ARTICLE

Renal Excretion of Water-soluble Contrast Media After Enema in the Neonatal Period

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newborn;
renal excretion;
water-soluble iodinated

Background: When abdominal distention occurs or bowel obstruction is suspected in the neonatal period, a water-soluble contrast enema is helpful for diagnostic and therapeutic purposes. The water-soluble contrast medium is evacuated through the anus as well as excreted via the kidneys in some babies. This study was designed to evaluate the incidence of renal excretion after enemas using water-soluble contrast media and presume the causes.

Methods: Contrast enemas using diluted water-soluble contrast media were performed in 23 patients under 2 months of age. After the enema, patients were followed with simple abdominal radiographs to assess the improvement in bowel distention, and we could also detect the presence of renal excretion of contrast media on the radiographs. Reviewing the medical records and imaging studies, including enemas and consecutive abdominal radiographs, we evaluated the incidence of renal excretion of water-soluble contrast media and counted the stay duration of contrast media in urinary tract, bladder, and colon.

Results: Among 23 patients, 12 patients (52%) experienced the renal excretion of water-soluble contrast media. In these patients, stay-in-bladder durations of contrast media were 1-3 days and stay-in-colon durations of contrast media were 1-10 days, while stay-in-colon durations of contrast media were 1-3 days in the patients not showing renal excretion of contrast media. The Mann-Whitney test for stay-in-colon durations demonstrated the later evacuation of contrast media in the patients with renal excretion of contrast media ($p = 0.07$). The review of the medical records showed that 19 patients were finally diagnosed as intestinal diseases, including Hirschsprung's disease, meconium ileum, meconium plug syndrome, and small bowel atresia or stenosis. Fisher's exact test between the presence of urinary excretion and intestinal diseases indicated a statistically significant difference ($p = 0.04$).

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Conclusion: The intestinal diseases causing bowel obstruction may increase the water-soluble contrast media's dwell time in the bowel and also increase urinary excretion.

1. Introduction

Diatrizoate meglumine is a water-soluble contrast medium for the gastrointestinal (GI) tract. Usually, it is indicated for the early postoperative assessment following GI surgery and the evaluation of suspected GI perforation.[1] This water-soluble contrast medium has been used in neonates for the treatment of uncomplicated meconium ileus, and it was believed to loosen the viscous, tenacious meconium through its hyperosmolar and water-soluble properties. Large volumes of fluid are drawn into the bowel, freeing the meconium and allowing it to pass through the rectum.[2–6] The patients who undergo water-soluble contrast enemas are followed with simple abdominal radiographs to evaluate the improvement in bowel distention and the effectiveness of enema. In some patients, we noticed that the urinary tracts, mainly urinary bladders, were opacified on the radiographs.

In this study, we evaluated the cases of water-soluble contrast enema in patients less than 2 months of age and divided them into two groups according to the presence of opacified urinary tracts on follow-up simple abdominal radiographs, which suggests renal excretion of contrast media. Then, we investigated the differences between the two groups and the causes of urinary tract opacification.

2. Methods

Since April 2004, 32 patients less than 1 year of age underwent contrast enemas with water-soluble contrast media at our institute: 10 examinations in 2004, four in 2005, two in 2006, two in 2007, 11 in 2008, two in 2009, and one in 2011. All studies were performed after obtaining documented informed consent from the parents or legal guardians. With retrospective review of the medical records and imaging studies, we excluded patients with uncertain diagnosis, patients lost to follow-up, patients with bowel perforation, and patients whose follow-up abdominal radiographs were not performed until the time when the instilled contrast media were completely evacuated. Finally, we enrolled 23 patients in this study and patients' demographics are presented in Table 1.

All 23 patients underwent water-soluble contrast enemas for severe abdominal distention or a lack of fecal evacuation in spite of saline or glycerin enemas. The contrast material used was diatrizoate meglumine and diatrizoate sodium solution (Gastrografin; Bayer Schering Pharma, Santa Rosa, Spain). It is a lemon-flavored, water-soluble, hyperosmolar (1750 mOsm/L), iodinated radiopaque contrast medium containing amidotrizoic acid 597 mg/mL, meglumine 159 mg/mL, sodium hydroxide 6 mg/mL, and bound iodine 367 mg/mL. Owing to the hyperosmolarity of the contrast media, patients received intravenous fluids to prevent any possible imbalance of fluid or electrolytes prior to the study. Contrast enemas were performed with the following procedure. A Foley catheter was placed in the rectum without ballooning, and the buttocks were strapped tightly together to prevent leakage of contrast. At the beginning of the study, all patients were positioned for a lateral view in order to evaluate the presence of the narrowing segment in the rectum

Table 1 Demographics of 23 patients according to excretory pathway of contrast.

Group			R group ($N = 12$)	NR group ($N = 11$)	p
Sex	Male	12 (52)	6 (50)	6 (55)	
	Female	11 (48)	6 (50)	5 (45)	
Gestational age	(wk)		28 ~ 41 (36 ± 2)	26 ~ 41 (35 ± 3)	0.33*
Maturity	Preterm	10 (43)	5 (42)	5 (45)	
	Term	19 (57)	7 (58)	6 (55)	
Birth weight	(g)		1340 ~ 4000 (2616 ± 507)	976 ~ 3840 (2296 ± 573)	0.24*
Delivery type	Vaginal	8 (35)	6 (50)	2 (18)	
	Cesarean	15 (65)	6 (50)	9 (82)	
Age at enema			0 ~ 30 days Birth ~ 1 wk 9 (75) 1 wk ~ 1 mo 2 (17) 1 mo ~ 1 (8)	1 ~ 65 days Birth ~ 1 wk 5 (45.5) 1 week ~ 1 mo 1 (9) 1 mo ~ 5 (45.5)	

The numbers in parentheses represent the percentages.
*Student *t* test.

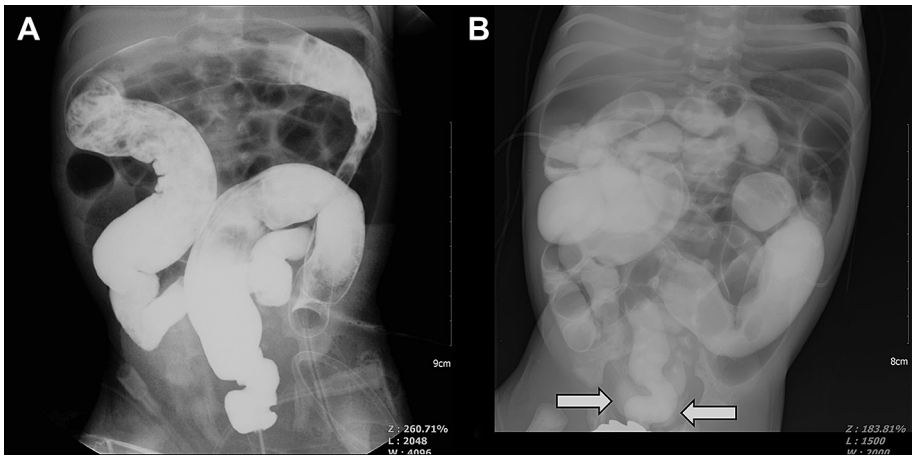

Figure 1 (A) A 4-day-old boy with abdominal distention. The colon study demonstrates multiple filling defects in descending and transverse colon, slowly refluxed into the proximal colon and terminal ileum by the pressure of injected contrast. (B) Supine abdominal radiograph taken 3 hours after the colon study demonstrated opacified urinary bladder.

and sigmoid, i.e., the transitional zone, which was helpful for diagnosing Hirschsprung's disease. Ten milliliters of Gastrografin diluted with 40 mL of warm saline (20% of solution) was prepared in a 50-mL enema syringe. Under fluoroscopic guidance, water-soluble contrast was gently infused by hand injection. The amount of instilled contrast media varied in each patient, from 20 to 100 mL of diluted contrast. The amount of contrast media was determined by the examiner during the procedure, according to the progression of contrast media. When small bowel dilatation was evident on the abdominal radiograph, or when meconium obstruction was suspected clinically, we tried to send the contrast media into the ileum via the ileocecal valve and finally to the dilated small bowel that was proximal to the obstructing meconium (Figure 1). Sometimes, if the transitional zone was ruled out at the beginning of the procedure, we inflated the Foley catheter balloon with 2–3 mL of air to send more contrast into the proximal bowel, resulting in more effective liquefaction of the inspissated meconium plug (Figure 2). After the enema, patients were followed with simple abdominal radiographs to assess the improvement in bowel distention and the effectiveness of the enema.

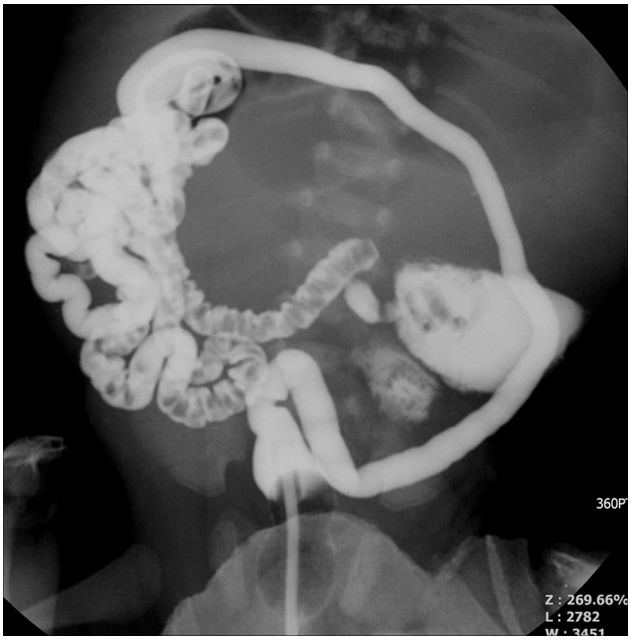

Figure 2 A preterm baby of 34 + 6 weeks gestational age who suffered from a disturbance in the meconium passage. The last film of the colon study reveals the absence of normal haustra and a greatly decreased caliber of the colon, suggesting microcolon. A rectal tube was inflated with 3 mL of air for effective reflux of Gastrografin into the small bowel. Finally, a dilated small bowel was opacified, after the long tubular filling defects in the distal ileum, which implied that the meconium plugs were refluxed.

One general radiologist and one pediatric radiologist retrospectively reviewed the images and follow-up abdominal radiographs in consensus. The renal excretion of water-soluble contrast media was defined when the urinary tracts, including bladders, were opacified on consecutive abdominal supine or lateral radiographs after enema (Figures 1 and 3). We divided the patients into two groups: patients experiencing renal excretion as well as anal evacuation of contrast media were categorized as group "R", and the remaining as group "NR", which means that renal excretion was not evident.

We reviewed the medical chart and imaging findings and analyzed the differences between the two groups using the Mann-Whitney rank sum test and Fisher's exact test. Two-tailed p values of <0.05 were considered significant. We utilized the MedCalc v.12.1.4 statistical software package (MedCalc Software, Mariakerke, Belgium) for analysis.

3. Results

Among the 23 patients who underwent enema with water-soluble contrast media, 12 patients (52%) showed an opacified urinary tract and bladder on follow-up abdominal radiographs after enema and were classified as the R group. The remaining 11 patients (48%) were assigned to the NR group (Table 1).

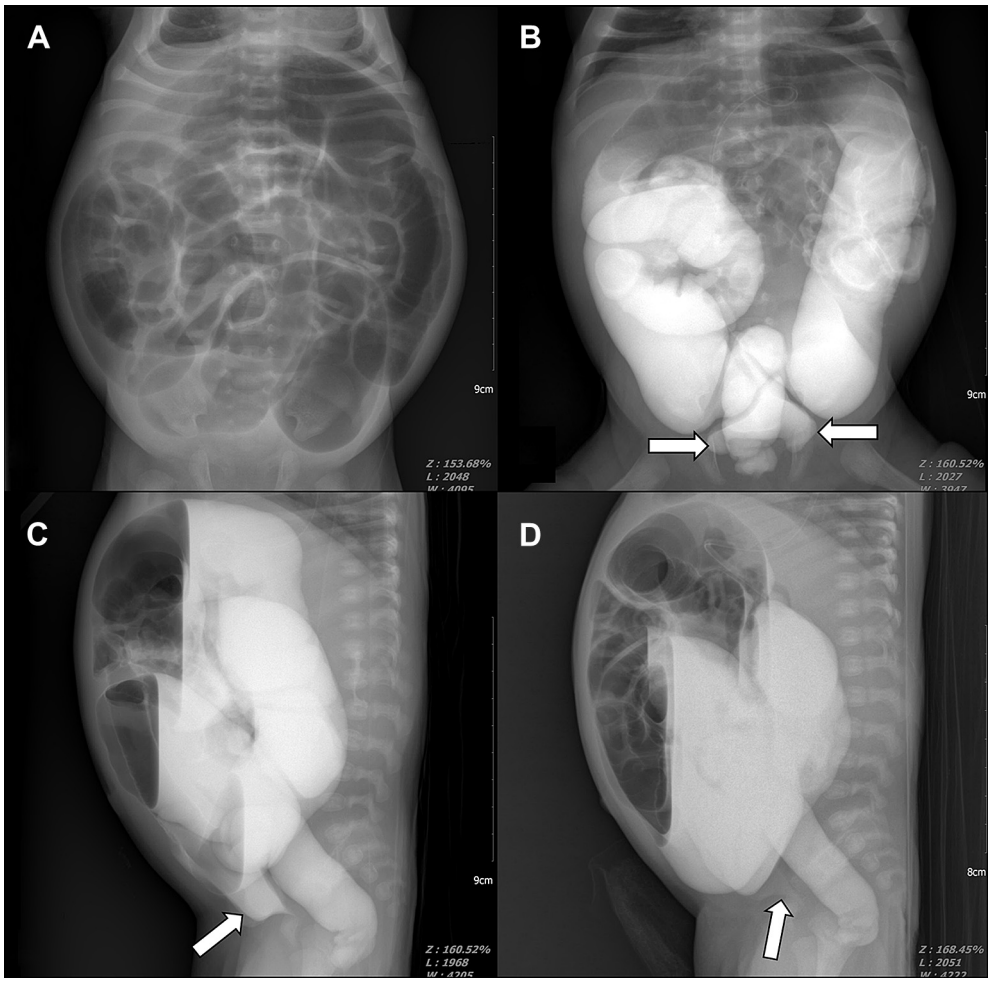

Figure 3 (A) A 28-day-old boy with severe abdominal distention. The initial supine abdominal radiograph shows abdominal bulging and gaseous distention of the bowel with no gas in the rectum. (B) Supine and (C) cross table lateral abdominal radiographs are taken 8 hours after the colon study. The contrast filled the colon, and the urinary bladder is opacified in front of the rectum that is demonstrated well on both views. (D) Cross table lateral abdominal radiograph taken on the next day of contrast study. Although the density is decreased, the urinary bladder is still visible. The patient was diagnosed with Hirschsprung's disease by rectal biopsy that revealed an absence of ganglion cells.

All 12 patients of the R group showed the opacified urinary bladder on abdominal radiographs. Among them, nine patients showed an opacified urinary bladder on both abdomen supine and lateral views, while three patients presented with an opacified bladder on only the lateral views. The days of stay-in-colon as well as stay-in-bladder were counted reviewing the abdominal radiographs. The results for each group are presented in Table 2.

In terms of the stay-in-colon duration, the Mann-Whitney test between the two groups presented the tendency of earlier evacuation of contrast in the NR group than in the R group; however, this was not statistically significant ($p = 0.07$).

In terms of the stay-in-bladder duration, the bladder was opacified and visible on the day of the enema in all 12 patients; visible to the next day in eight patients; visible to the 3rd day in four patients; and not depicted after the 4th day.

A review of medical records determined final diagnoses, which included various congenital GI diseases, such as six patients with Hirschsprung's disease, including one case with total aganglionosis, five with meconium ileus, four with meconium plug syndrome, one with ileal atresia, one with ileal stenosis, one with duodenal atresia, and one with jejunal atresia. All 12 patients of the R group had the above mentioned congenital GI diseases. Seven patients (64%) of the NR group were proved to have congenital GI diseases, but not in the remaining four patients. Fisher's exact test between the presence of urinary excretion and the diagnosed congenital GI disease was performed. The resulting p value was 0.037 with 100% of sensitivity, 36.4% of specificity, 63.2% of the positive predictive value, and 100% of the negative predictive value, which indicated that there was a statistically significant difference in the presence of urinary excretion and GI diseases (Table 2).

4. Discussion

Non-surgical treatment of meconium ileus was first attempted using hydrogen peroxide in 1954 by Olim et al[4] Dr Noblett

Table 2 Findings on follow-up abdominal radiographs and medical record data according to excretory pathway of contrast.

Group	R group ($N = 12$)	NR group ($N = 11$)	p
Stay-in-colon duration of contrast	1∼10 d ∼1st d 4 (33.3%) ∼3rd d 4 (33.3%) 4th d∼ 4 (33.3%)	1∼3 d ∼ 1st d 7 (63.6%) ∼ 3rd d 4 (36.4%) 4th d∼ 0	0.07*
Stay-in-bladder duration of contrast	1∼3 d ∼1st d 4 (33.3%) ∼2nd d 4 (33.3%) ∼3rd d 4 (33.3%)		
Presence of intestinal problem	12 (100%)	7 (64%)	0.04†

*Mann-Whitney test.
†Fisher's exact test.

reported the use of Gastrografin for four patients with meconium ileus in 1969 and emphasized the importance of administering a radiopaque agent with fluoroscopic control for safety concerns.[3] Later, several articles also reported the use of Gastrografin for the treatment of uncomplicated meconium ileus, especially in neonates and young infants.[2–6] Gastrografin is believed to be successful in relieving the intestinal obstruction in meconium ileus because of its high osmolarity that draws fluid into the bowel lumen from the plasma, which has an osmolarity of 280∼300 mOsm/L, thereby loosening the viscous, tenacious meconium. In addition to the hypertonic nature of the contrast medium, the wetting agent is thought to lubricate the meconium and facilitate its passage to the distal bowel.[3] In our institution, water-soluble contrast enema is performed for neonates and young infants who require relief from intestinal obstruction due to a meconium plug or rarely meconium ileus that is not relieved with glycerin or saline enema. Diatrizoate meglumine may carry some risk of dehydration, resulting in an increased hematocrit, rising serum osmolarity, and reduction in pulse rate and cardiac output.[5] Therefore, careful attention regarding sufficient hydration is necessary before, during, and after the procedure.

After water-soluble contrast enema, most of the water-soluble contrast media is evacuated via the rectum, and absorption from the intestine is minimal. Then, how to explain the opacified urinary tracts (mostly urinary bladders) in some patients of our study? Since the report by Mori and Barrett in 1962,[7] the presence of ingested water-soluble contrast media in the urinary tract, as detected on abdominal radiographs, has been regarded as a strongly suggestive finding of gastrointestinal perforation or anastomotic leakage after gastrointestinal surgery.[1] In these cases, orally administered water-soluble contrast media may leak into the peritoneum and may be absorbed into the blood stream and then be excreted by the kidneys. However, since the introduction of computed tomography (CT), one report presented the urinary excretion of orally administered water-soluble contrast media observed on CT in patients with various bowel diseases and had no perforation.[8] Our patients in the R group showed no free air in the abdomen cross table lateral views. Therefore, we assumed that the urinary excretion of Gastrografin in the R group was mainly because of the absorption from the intestinal wall rather than bowel perforation. We admit the limitation of abdominal radiographs compared with CT to show excreted contrast because CT is a more sensitive modality for identifying the presence of urinary excretion of contrast media. However, if performed, CT has a limitation in neonates and young infants owing to the radiation hazard.

In our results, the stay-in-colon duration of contrast media after the colon study was longer in the R group than in the NR group, but this was not statistically significant ($p = 0.07$; Table 2). The patients in the R group had more probability of the presence of GI diseases than that of the patients in the NR group ($p = 0.04$; Table 2). Therefore, for the R group, we assumed that the longer stay-in-colon duration was related to or caused by the GI diseases, resulting in colonic obstruction, which led to more Gastrografin being absorbed from the intestinal wall.

What is the proper amount of diatrizoate meglumine used for enemas in neonates and young infants? Few reports have described the precise amount of diatrizoate meglumine used for enemas in neonates and young infants. O'Halloran et al[2] reported that the majority of children who required Gastrografin enemas to relieve meconium ileus had been given 100-200 mL of Gastrografin in three times the volume of water under fluoroscopic control. Garza-Cox et al[9] stated that up to 20 mL of solution was generally sufficient to outline the colon, distal ileum, and inspissated meconium plugs on plain abdominal radiographs in very low birth weight premature infants. In our study, although the amount was different in each case, we instilled 20—100 mL of diluted contrast, which was not a large amount, considering the gestational age of the enrolled patients.

Bowel perforation is a representative, but not commonly occurring, complication of contrast enema in children. A survey by Kao and Franken[10] demonstrated 2.75% of perforation, and its occurrence was not correlated with the success rate of the enema or properties of the contrast medium. The only high risk factor for rectal perforation was reported to be the use of an inflated balloon catheter, similar to our result. We experienced one unfortunate case with rectal perforation, although we did not enroll the patient in the current study. This patient was a male of 37 + 2 weeks of gestational age and his initial body weight was 2900 g. He underwent colon study on the 5th day of life. The Foley catheter balloon was inflated from the beginning of the colon study due to the inexperience of the examiner.

In conclusion, an opacified urinary tract and bladder can be observed on follow-up abdominal radiographs after water-soluble contrast enema in neonates and young infants. The GI diseases causing colonic obstruction may increase water-soluble contrast dwell time in the bowel and increase urinary excretion.

Contributors

Bo-Kyung Je designed the study and data collection tools, monitored data collection for the whole trial, wrote the statistical analysis plan, and cleaned and analysed the data. Hee Sun Kim wrote the statistical analysis plan and monitored data collection for the whole trial. Bo-Kyung Je, Sang Hoon Cha, Ki Yeol Lee, and Seung Hwa Lee performed the radiologic examination and read the radiographs. Byung Min Choi made the clinical diagnosis and monitored the patients' data. Bo-Kyung Je and Hee Sun Kim drafted the paper. Bo-Kyung Je, Sang Hoon Cha and Byung Min Choi revised the draft paper.

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Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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